Annals of Gastroenterology (2024) **37,** 1-8

Paraduodenal pancreatitis as diagnostic challenge: clinical and morphological features of patients with pancreatic pathology involving the pancreatic groove

Francesco Vitali[a,b], Marc Heinrich[c], Deike Strobel[a], Sebastian Zundler[a], Ali A. Aghdassi[b], Michael Uder[c], Markus F. Neurath[a], Robert Gruetzmann[d], Marco Wiesmueller[c], Luca Frulloni[e], Dane Wildner[a]

University Hospital of Erlangen, Germany; University Medicine of Greifswald, Germany; University of Verona, Italy

Abstract

Background Paraduodenal pancreatitis (PP) is an inflammation involving the groove zone, delimited by the duodenum lumen, bile duct, and the head of the pancreas. This area may also be involved during acute pancreatitis (AP). The differential diagnosis is clinically relevant, since PP generally persists, whereas AP resolves. Hence, we compared a cohort of patients with PP and AP involving the groove area.

Methods We retrospectively evaluated patients with pathology involving the groove area. The primary aim was to define the diagnostic features of PP compared to non-PP pancreatitis involving the groove area. PP was diagnosed by imaging, while AP was diagnosed according to the revised Atlanta classification and the clinical course, to exclude chronic pancreatitis.

Results The study population consisted of 37 patients (32 men, age 56.9±9.1 years), 25 with a diagnosis of PP (23 men, mean age 54.9±8.5 years), and 12 (9 men, mean age 61.2±9.2 years) with AP involving the groove. All 25 patients with PP and 4 (33.3%) with AP reported a history of alcohol abuse, 23 patients (92%) with PP, and 3 (25%) with AP had a history of smoking. On imaging, PP patients presented a significantly thicker duodenal wall compared to the AP group (P=0.010). Chronic pancreatitis in the body/tail and exocrine insufficiency was prevalent in PP (P<0.001 and P=0.02). The medial displacement of the gastroduodenal artery was more frequent in the PP group (P=0.011).

Conclusion PP has a different clinical and imaging profile compared to AP involving the groove area.

Keywords Paraduodenal pancreatitis, mass forming chronic pancreatitis, pancreatic necrosis, groove pancreatitis

Ann Gastroenterol 2024; 37 (XX): 1-8

[a]First Department of Medicine, University Hospital of Erlangen, Germany (Francesco Vitali, Deike Strobel, Sebastian Zundler, Markus F. Neurath, Dane Wildner); [b]Department of Medicine A, University Medicine of Greifswald, Germany (Francesco Vitali, Ali A. Aghdassi); [c]Department of Radiology, University Hospital of Erlangen, Germany (Marc Heinrich, Michael Uder, Markus Wiesmueller); [d]Department of Visceral and General Surgery, University Hospital of Erlangen, Germany (Robert Gruetzmann); [e]Istituto del Pancreas, University of Verona. Verona, Italy (Luca Frulloni)

Conflict of Interest: None

Correspondence to: Francesco Vitali MD, First Department of Medicine, University Hospital of Erlangen, Friedrich-Alexander-University Erlangen-Nuremberg, Ulmenweg 18, 91054 Erlangen, Germany, e-mail: francescovitalimd@gmail.com

Received 18 April 2024; accepted 15 July 2024;
published online 20 October 2024

DOI: https://doi.org/10.20524/aog.2024.0914

Introduction

Chronic pancreatitis is a progressive fibro-inflammatory disease of the pancreas that in the final stage leads to irreversible pancreatic atrophy, resulting in pain, and exocrine and endocrine insufficiency [1]. In the last decades, rare forms of chronic pancreatitis, namely autoimmune pancreatitis [2] and paraduodenal pancreatitis (PP) [3], have been identified as distinct entities. In 2002 the World Health Organization classification acknowledged the term "para-duodenal wall cyst" [4]. The onset of PP occurs in the anatomical compartment of the pancreatic groove: the space between the duodenum, the pancreatic head and the intrapancreatic bile duct.

PP is a rare form of chronic pancreatitis that has been described in the literature under various names, such as "Rinnenpankreatitis" [5-8], "cystic dystrophy of the duodenal wall" in French or Italian papers [9-12], "groove pancreatitis" in other countries [13,14], or "pancreatic hamartoma of the duodenal wall" [15,16]. The pathological features of PP are well defined and the term "paraduodenal pancreatitis" was

proposed to encompass all these different entities, which have been morphologically classified as either a cystic or solid form of PP [3]. PP can be diffuse, involving the body and tail of the pancreas, or focal, localized in the groove with preservation of the pancreatic parenchyma. It can also be found in a pure form confined to the pancreatoduodenal groove, mimicking a periampullary tumor. A more recent classification published by Muraki *et al* more precisely defined the subtypes of PP, also based on the postulated pathophysiological mechanism [17].

It is postulated that pancreatic tissue in the duodenal wall at the level of the minor papilla may result from abnormal migration of the dorsal pancreatic bud. This heterotopic pancreas, associated with abnormalities in the duct system [3], may be more sensitive to exogenous factors, particularly alcohol. Indeed, alcohol and tobacco have been associated with PP [18]. These noxae act on the heterotopic pancreas in the groove, on the small pancreatic ducts or the duct of Santorini, or on the local vessels, particularly the arterioles [19], triggering a self-enhancing acute or chronic inflammation process that represents a common injury pattern for PP [17].

The spectrum of clinical findings in PP is quite restricted, since it occurs mainly in middle-aged men with a history of tobacco and alcohol abuse [20]. The most common symptom is upper abdominal pancreatic pain, often continuous and severe. Clinically and on imaging, duodenal stenosis, periampullary cysts, jaundice or obstructive pancreatitis can occur in varying degrees, as well as space-occupying lesions that functionally act as a periampullary mass mimicking cancer [17]. Accordingly, the imaging features of PP are diverse, ranging from a space-occupying lesion resembling cancer to paraduodenal cystic lesions that may mimic pancreatic cystic neoplasms or duodenal duplication (Fig. 1A). This heterogenous spectrum of findings leads to an over-diagnosis of possible malignancy and to a high rate of surgery [21,22]. In fact, PP accounts for 3-5% of pancreatic head resections performed because of the suspicion of pancreatic head or periampullary cancer [17,23]. The diagnosis of PP can be made using imaging techniques [10-12,23-25], but the gold standard is still pathological examination [3,26]. Endoscopic ultrasound (EUS) may demonstrate a thickened duodenal wall, particularly involving the submucosa and *muscularis propria*, sometimes with loss of wall stratification (in the acute recurrent inflammatory phase) or with the presence of cysts inside [27,28]. Upon EUS contrast medium application, areas around the cyst are not enhanced and the surrounding thickened wall shows patchy and delayed enhancement, as well as a hard appearance on elastography [29], making the differential diagnosis with groove carcinoma, duodenal carcinomas or highly proliferative necrotizing neuroendocrine tumors difficult. Endoscopic findings show a congested, edematous, and erythematous mucosa in the second part of the duodenum around the major papilla [30]. A duodenal stenosis can also occur, making an EUS examination challenging.

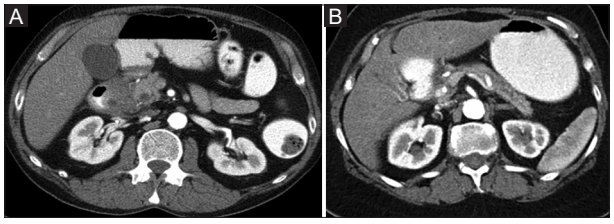

Figure 1 (A) Contrast medium-enhanced computed tomography (CT) scan in the arterial phase, showing a hypodense mass forming paraduodenal pancreatitis with thickening of the duodenal wall, duodenal cysts, medial displacement of the gastroduodenal artery, duodenal stenosis and stomach dilation, with stasis of the oral contrast medium. (B) Contrast medium-enhanced CT scan in the arterial phase showing a hypodense mass in the groove and duodenal thickening as a consequence of pancreatic groove necrosis.

PP has mostly been described in surgically treated cohorts [17,21,23], and long-term outcomes, especially in those patients managed medically, are poorly described in the literature and presented only in retrospective analyses [14,20,31]. Since other conditions that affect the groove area can present with clinical features similar to those of PP, we compared our cohort of patients with PP to a group of patients presenting with acute pancreatitis (AP) involving the pancreatic groove area (Fig. 1B) to analyze the optimal diagnostic criteria for these conditions and the outcome of the therapeutic choices. The aim of this study was also to find potential differences that can help distinguish these 2 conditions prior to surgery and facilitate tailored treatment, avoiding misdiagnosis of cancer.

Patients and methods

We retrospectively evaluated the clinical records of patients who were managed in the University Hospital of Erlangen (Germany) after a diagnosis of a new-onset pancreatic pathology involving the groove area on imaging, defined at the first imaging evaluation and re-evaluated by 2 radiologists blinded to the clinical data (MH and MW). We analyzed clinical, surgical and radiological data, and hospital readmissions using our prospective clinical database ("Soarian") (Siemens GmbH, Erlangen) from January 1, 2005 up to December 31, 2022. The diagnosis of PP was based on imaging (computed tomography [CT] and/or magnetic resonance [MRI]) or histology (Supplementary Table 1). The primary aim was to define the diagnostic features of PP compared to similar conditions involving the groove area, namely AP with groove necrosis. Secondary aims were to compare clinical and radiological data and outcomes of conservative, interventional and surgical therapies for pancreatitis involving the groove area. Diagnosis of PP was done according imaging [10,12] and where available, histopathology [3]. The diagnosis of AP was made according to the revised Atlanta classification [32], and patients were assigned to the AP group *a posteriori*, taking into account their clinical course and medical history to exclude chronic pancreatitis.

Data collection

The following clinical parameters were collected: age at clinical onset; sex; alcohol consumption (none <10 g/day,

medium 10-20 g/day, abuse >20 g/day); cigarette smoking (none, <10 pack years, >10 pack years); jaundice; vomiting; weight loss (defined as a reduction by >10% of the normal body weight within 6 months); endocrine pancreatic insufficiency (fasting serum glucose >126 mg/dL); exocrine pancreatic insufficiency (clinical detectable steatorrhea or fecal elastase 1 <100 μg/g of stools); AP, defined as upper abdominal pain and an increase in serum lipase to greater than 3 times the upper normal limit; cancer antigen 19-9; jaundice; and a diagnosis of liver cirrhosis or portal and/or splenic vein thrombosis. The suspicion of cancer was recorded according to the judgment of a multidisciplinary board. Readmission for recurrence of pancreatic disease during the follow up was also recorded from the diagnosis.

Endoscopic and surgical procedures

The performance of endoscopic retrograde cholangiopancreatography (ERCP), duodenal dilation procedures, duodenal stenting, transpapillary drainage, EUS cyst drainage, fine-needle aspiration, and bile duct or pancreatic duct stenting were recorded. The type and timing of surgery were recorded.

Radiological and histological data

All patients underwent CT and or MRI with intravenous contrast agents. The following data were recorded: duodenal stenosis, stomach dilation, nodular lesions suggesting heterotopic pancreas, pancreatic calcifications, peripancreatic effusions, lymphadenopathy, acute inflammation, pancreatic head enlargement, double duct sign, suspicion of cancer, number and size of duodenal wall cysts, main pancreatic duct dilation, bile duct, pseudocyst in the pancreatic body and tail, and chronic pancreatitis of the pancreas outside the groove area. Duodenal wall thickening was measured in mm and the extension of the thickening was described as localized in the pylorus, duodenal bulb, descending part of the duodenum, or medial part. Contrast medium enhancement in the arterial and venous phase was recorded. PP has been classified as "solid" or "cystic", according to the radiological presence of cysts in the duodenal wall (as in previous reports [20], Fig. 2), or to a histopathological diagnosis of microcysts (<1 cm) in the solid type or macrocysts (>1 cm, usually detectable on CT) in the cystic type (as in other reports [23]).

The pure or diffuse type was diagnosed according to the involvement of the pancreas itself (with calcification, pancreatic duct dilation, parenchyma atrophy) outside the groove area. The classification of Muraki *et al* was applied to our cohort of patients with PP [17]. Histological diagnosis of surgical specimens was carried out according to previously published criteria [3].

Statistical analysis

General characteristics are expressed as median and range. Statistical analysis was performed using the analysis of variance test and Student's *t*-test with Yates' correlation for parametric variables. The Mann-Whitney *U* test was used for continuous data. A χ^2 analysis was used for categorical variables. The Fisher exact probability test was used for the 2×2 contingency tables, where appropriate. The data were analyzed using the SPSS 26 statistical software (IBM Corp., Armonk, New York, USA). All statistical tests were 2-sided. P-values <0.05 were considered to be statistically significant.

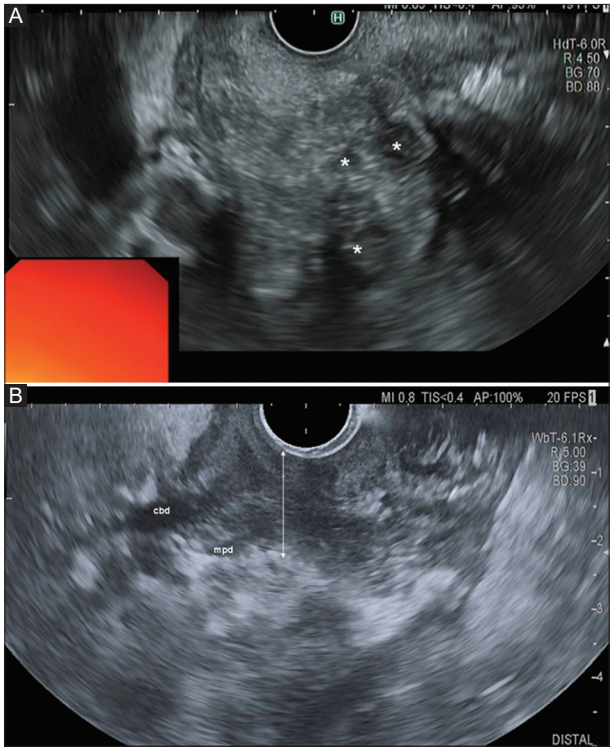

Figure 2 Endoscopic ultrasound images of a paraduodenal pancreatitis. (A) Duodenal wall thickening visualized with the linear echoendoscope, with multiple cysts within the duodenal wall (*). (B) Duodenal wall thickening (double arrow) visualized in the *pars descendens duodeni* with the radial echoendoscope *Cbd, common bile duct; mpd, main pancreatic duct*

Results

The final study population consisted of 37 patients, predominantly men (n=32) with a mean age of 56.9±9.1 years. Body mass index was 24.2±4.1 kg/m^2. Of these patients, 25 were diagnosed with PP, while 12 patients presented with pancreatic necrosis involving the groove (group AP). In the PP group, 9 patients (36%) presented with the cystic form of PP and 16 with the solid variant (64%); 21 (84%) patients presented with diffuse chronic pancreatitis; 3 (12%) patients presented a localized pancreatitis in the groove (pure form) solid variant (1A), 5 (20%) type 1B according the Muraki *et al* classification (Table 1).

The clinical and radiological characteristics of the study population, together with a comparison between the 2

Table 1 Classification of PDP in our cohort according to Muraki *et al* [17], compared to the terminology (*italics*) found in the literature

Subtype	Number total n=25	%
1A *groove-predominant pattern (sandwich pattern)* – pure form	3	12
1B *pancreas-involving pattern (rice ball pattern)* – segmental form	5	20
2A Cyst-Forming Type of PDP - groove-predominant cystic pattern	3	12
2B *Cyst-Forming Type of PDP* - pancreas-predominant cystic pattern	14	56

PDP, paraduodenal pancreatitis

groups, are shown on Table 2. All patients with PP reported a history of alcohol abuse (in the AP group 66.7% were non-drinkers), 23 (92%) were smokers, 17 (68%) presented with weight loss, 14 (56%) presented with abdominal pain and 12 (48%) presented with jaundice. Exocrine pancreatic insufficiency was present in 13 (52%) and 14 (56%) patients had duodenal stenosis. Re-hospitalization was necessary in 12 patients (48%), while 23 (92%) of the PP group presented with pancreatic head enlargement on imaging. A suspicion of cancer was present in 13 patients (52%) and tumor marker elevation was seen in 4 (16%). The median follow up of the PP group was 46±34.1 months. Twenty patients were managed conservatively, 20 (80%) underwent endoscopic therapy, 17 underwent surgery (9 duodenopancreatectomy, 7 duodenum-preserving pancreatic head resection, 1 gastroenterostomy). Twenty underwent ERCP (9 with pancreatic stenting), 2 transpapillary drainage, 6 duodenal dilation, 3 duodenal metal stenting and 2 EUS-guided drainage. Six patients underwent fine-needle aspiration, 4 with inconclusive results.

In the AP group, endoscopic therapy was performed in 10 patients (83%) and operative therapy in 3 (duodenopancreatectomy), 2 patients underwent duodenal stenting. Three patients (16%) presented elevated tumor markers. Taking both groups altogether, serum tumor markers were elevated in 7 patients (19%).

On imaging, the PP group showed a significantly thicker duodenal wall in comparison to the AP group (P=0.010). Chronic pancreatitis in the body/tail and exocrine insufficiency was more frequent in the PP group (P<0.001 and P=0.02). Medial displacement of the gastroduodenal artery was more frequent in the PP group (P=0.011). Heavy smoking and drinking were more common in PP patients (P<0.001). The follow up was significantly longer in the PP group than in the AP group (46.6 vs. 17.6 months P=0.008).

Discussion

PP represents a diagnosis and management challenge for clinicians, radiologists and surgeons. Numerous studies have been published concerning the diagnostic criteria for radiological diagnosis, differential diagnosis and treatment algorithms based on clinical and surgical cohorts [10-12,14,18,20,22,24,25,31,33]. Its various appearances on imaging, as a solid or cystic lesion involving different adjacent structures, including the duodenum, stomach, bile duct and pancreatic duct, mean that its clinical onset can be heterogeneous [34].

The most important and challenging differential diagnosis is between PP and periampullary or pancreatic cancer [35-37]. A retrospective multicenter study from Finland emphasized this aspect, showing that diagnosing PP based on imaging only, without relying on clinical data, may lead to error, even when there is high certainty of PP among specialized radiologists [31]. Some diagnostic radiologic criteria have been published that differentiate PP from groove pancreatic neoplasms on both CT and MRI [38,39]. However, resective surgery (duodenopancreatectomy) is still performed in cases of PP where cancer cannot be definitively ruled out [21,23].

In this study, we found different clinical and, eventually, radiological features that helped with the differentiation between 2 other entities: PP and groove pancreatic necrosis (Fig. 1A and B). Despite the low number of cases collected, data were analyzed retrospectively over a long period. These 2 rare conditions somehow overlap, having similar radiological appearance and clinical management. In patients with PP, we found numerically higher rates of recurrence, though the difference was not statistically significant because of the small sample. We also showed that PP needed more ERCP sessions. This result stresses that PP is a chronic recurrent disease that may deteriorate. If the cysts or the thickness of the groove evolve as a result of chronic inflammation, further interventions may become necessary, for instance due to stent displacement. That was also common in the mainly endoscopically treated cohort reported by Arvanitakis *et al* [25], where 60% of the patients required endotherapy for more than 2 years.

In view of the unique pathogenesis of PP, which involves a combination of factors such as pancreatic heterotopia, pancreatic outlet flow obstruction at the level of the minor papilla, complete or incomplete pancreas divisum, and local ischemic damage as a consequence of alcohol or nicotine excess, the authors believe that the patients' history should be taken in account as a primary criterion to strengthen diagnosis. This was also shown in other studies, where cancer was misdiagnosed as PP in non-smokers [33] and females [38]. In addition, in our cases PP was significantly more frequent in patients presenting with alcohol abuse and smoking excess. We did not observe any sex-related differences.

There is ongoing debate as to whether PP represents a separate entity or a subset of alcoholic chronic pancreatitis, classified by Muraki *et al* as an "ill-defined type of paraduodenal pancreatitis". In our cohort, none of our patients were classified in this category. This could be due to the strict radiological inclusion criteria, or because such patients do not become clinically symptomatic because of the mass-forming effect of the inflammation in the groove area, but the most probable explanation is the damage to

Table 2 Comparison of clinical and radiological findings between patients with paraduodenal pancreatitis and acute pancreatitis (pancreatic groove necrosis)

Findings n=37	Paraduodenal pancreatitis n=25	Pancreatic groove necrosis n=12	P-value
Median age	54.9±8.5	61.2±9.2	0.17
Male sex	23	9	0.29
Body mass index	23.8±4.2	25.1± 4.0	0.32
Alcohol abuse	25	4	<0.001
Smoke abuse	23	3	0.003
Liver cirrhosis	3	0	0.25
Splenoportal vein thrombosis	3	0	0.25
Surgery	17	5	0.11
Other site cancer	5	1	0.67
Tumor marker elevation	4	3	0.52
Cancer antigen 19-9 U/mL	43.8±102.8	80.6 ± 182.6	0.33
Jaundice	12	3	0.18
Weight loss	17	8	0.64
Acute pancreatitis	14	6	0.59
Hyperlipasemia	14	6	0.78
Continuous pain	14	9	0.26
Recurrence	12	3	0.45
Worsening in follow up	10	2	0.49
Diabetes	10	3	0.08
Exocrine insufficiency	13	1	0.02
ERCP number	3.9±4.7	1.6±3.7	0.04
Pancreatic stenting	8	1	0.18
Duodenal stenting	1	2	0.11
Endoscopic duodenal dilation	6	0	0.08
Duodenal wall thickening >9 mm	20	9	0.97
Duodenal wall thickness (mm)	14.3±6.1	8.2±3.5	0.010
GDA displaced	16	2	0.011
Chronic pancreatitis of the body/tail	22	2	<0.001
Common bile duct dilation	13	3	0.18
Pancreatic duct dilation	14	3	0.18
Double duct sign	9	3	0.49
Calcifications	11	3	0.59
Duodenal stenosis	14	7	0.59
Pancreatic head enlargement	23	2	0.11
Follow up (months)	46.6±32.5	17.6±25.6	0.008

ERCP, endoscopic retrograde cholangiopancreatography; GDA, gastroduodenal artery

the pancreas itself, with consequent pain, symptomatic calcifications in the pancreatic body or tail, pancreatic atrophy and diabetes. Like other series [20], we also report only 3 patients with calcification of the pancreatic groove, but not of the body tail. If we embrace the hypothesis that the groove is the pacemaker of chronic pancreatitis [20], where the onset of disease is in the pancreatic head at the level of the groove and the chronically recurring inflammation precedes damage to the rest of the pancreas, PP was mostly diagnosed in the late stage in the PP group. Conversely, in the AP group the disease is localized solely to the groove and leads to acute symptoms that require rapid treatment, resulting in a long-

term improvement of symptoms and the avoidance of organ failure in the majority of cases.

The follow up was significantly longer in the PP group than in the AP group (P=0.008), demonstrating a more therapeutically demanding disease with a higher rate of recurrence: mean 12, compared to a mean of 3 in the AP group. That high number of all-cause readmissions was also seen in the cohort of Ooka *et al* [14]. A high recurrence rate (mean 5) was also reported by De Pretis *et al* [20], which may explain the high surgical rate as in our cohort.

Histological diagnosis was confirmed with histopathological analysis of the surgical specimens (duodenopancreatectomy in 6 cases and duodenal-sparing pancreatic head resection in 7), others were diagnosed by imaging, according to the criteria presented in Supplementary Table 1. The lack of histological examination in all patients is a shortcoming of our study, as it is for many other studies published on PP, although imaging has been accepted as a valid diagnostic tool and as an inclusion criterion in other studies [40-42]. To the best of our knowledge, there is a gap in the literature regarding studies of sensitivity, specificity and accuracy in the various diagnostic imaging modalities of PP, based on histopathological criteria and involving a large population of patients. This would require a multicenter prospective study, where all patients systematically undergo contrast-enhanced CT, MRI and EUS before surgery.

Therapeutic approaches include alcohol and nicotine withdrawal as a first conservative therapeutic step [11,18,20,31]. The efficacy of a therapy with somatostatin analogs is a matter of debate and not accepted in all countries, but it is reported to be effective as monotherapy, or combined with endoscopic therapy [11,25]. In cases of symptomatic cysts, jaundice or duodenal obstruction, endoscopic therapy offers a second therapeutic approach. The technique of cyst fenestration can involve a biopsy and aspiration of the cysts, or fenestration with a needle-knife. In the case of large cysts, drainage can be performed via placement of a prosthesis. Some data from Asia report on the efficacy of the drainage of the Santorini duct in order to reduce the outflow pressure on side branches in the inflamed groove area [12,43,44]. This technique is very demanding and data on safety are scarce.

If a step-up approach is undertaken and endoscopic techniques are successful and performed at qualified centers, a minority of patients will require surgery [25]. As reported by previous studies, the cystic variant does not necessarily need surgery, as up to 73% patients can be managed conservatively [11]. Although the incidence of surgery does not differ between the cystic and the solid variant [20], resective surgery is still the first treatment option in patients with a suspicion of cancer. In a worldwide survey among pancreatologists, 67% of specialists preferred duodenopancreatectomy as a first-line treatment, suggesting that experience of conservative or endoscopic therapy is not yet widespread [45], while a systemic review from 2017 reported a low rate (19%) of endoscopic treatment [46]. In our patients, endoscopic therapy was performed in 83% of the PP group, but it was also a relevant treatment option (80%) for patients with pancreatic groove necrosis (AP group). Whereas other series suggested surgery for duodenal obstruction [47], newer series consider endoscopic therapy for such benign conditions [48], although no comparative studies have yet been published.

In our study, 68% (17 patients) of the patients with PP eventually underwent surgical treatment. This is similar to the percentage reported in the mixed surgical–clinical series from Depretis *et al* [20]. Surgery with duodenopancreatectomy may be a general therapy for patients in whom cancer cannot be excluded, or in cases where conservative therapy fails [22]. In our AP group, 41% of the patients needed surgery, also because of the failure of conservative therapy, and in the cases where cancer could not be excluded.

Our study has several limitations. First, although clinical data were collected in a prospective database, the sample size was small, while in such a retrospective study all the linked biases of analyses have to be acknowledged. The recruitment criterion was mainly based on imaging for the PP group, so some cases of PP may have been overlooked. On the other hand, the long follow up is likely to have ruled out a malignant diagnosis in our cohort, while the clinical course should have excluded chronic pancreatitis in the AP group. PP is a rare disease, and since the diagnosis is complex and cases are still misclassified in clinical practice, to design a prospective study without evidence-based diagnostic criteria has been difficult thus far. We agree, however, with the statement of Muraki *et al*, that the correct classification and the recognition of different subtypes can tailor management according to the putative pathophysiological mechanisms [17]. Surgery, in particular duodenopancreatectomy, seems to be the most accepted procedure so far. A possible alterative could be pancreas-preserving duodenal resections for the treatment of paraduodenal pancreatitis type-2, although experience reported in the literature is from only 1 center [47].

In conclusion, pathology and inflammation in the groove act as a unique complex syndrome with many facets and different clinical approaches that, up to now, still remain to be investigated. PP is a disease characterized by various clinical aspects and typical radiological features that in some cases mimic cancer. Diagnosis can be achieved by imaging and EUS, which allows better classification of the subtypes of the disease (solid and cystic variants, as well the pure and diffuse forms). The onset of pancreatic necrosis in the groove area is an important differential diagnosis to consider. The management is similar, but PP is more demanding in terms of recurrences and progression with organ failure rates. Resective surgery, namely duodenopancreatectomy, may be a valid option in cases that are refractory to therapy, and where there is suspicion of malignancy. Given the rarity of this condition, large-scale studies including of mixed clinical and surgical cohorts will be needed to define the precise diagnostic criteria, subtypes, risk factors and subtype-tailored interdisciplinary management.

Summary Box

What is already known:

- Paraduodenal pancreatitis (PP) is an inflammation involving the groove zone, delimited by the duodenum lumen, bile duct and the head of the pancreas
- The diagnosis of PP can be made using imaging, although surgical pathology is the gold standard
- Differentiating between PP, malignancy and acute necrotic inflammation of the groove is challenging

What the new findings are:

- Radiological signs, such as duodenal wall thickening and medial displacement of the gastroduodenal artery, can help differentiate PP from acute necrosis of the pancreatic groove during acute pancreatitis
- Medical history of alcohol abuse, smoking and pancreatic insufficiency support the diagnosis of PP over other conditions occurring in the groove area

References

1. Beyer G, Habtezion A, Werner J, Lerch MM, Mayerle J. Chronic pancreatitis. *Lancet* 2020;**396**:499-512.
2. Finkelberg DL, Sahani D, Deshpande V, Brugge WR. Autoimmune pancreatitis. *N Engl J Med* 2006;**355**:2670-2676.
3. Adsay NV, Zamboni G. Paraduodenal pancreatitis: a clinico-pathologically distinct entity unifying "cystic dystrophy of heterotopic pancreas", "para-duodenal wall cyst", and "groove pancreatitis". *Semin Diagn Pathol* 2004;**21**:247-254.
4. Klöppel G. Histological typing of tumours of the exocrine pancreas. Springer Science & Business Media; 1996.
5. Stolte M, Weiss W, Volkholz H, Rosch W. A special form of segmental pancreatitis: "groove pancreatitis". *Hepatogastroenterology* 1982;**29**:198-208.
6. Seitz K, Rettenmaier G, Stolte M. [Groove pancreatitis—its pathological anatomy and sonographic findings]. *Ultraschall Med* 1985;**6**:131-133.
7. Becker V, Mischke U. Groove pancreatitis. *Int J Pancreatol* 1991;**10**:173-182.
8. Becker V. [Groove pancreatitis]. *Pathologe* 1992;**13**:199-203.
9. Potet F, Duclert N. [Cystic dystrophy on aberrant pancreas of the duodenal wall]. *Arch Fr Mal App Dig* 1970;**59**:223-238.
10. Procacci C, Graziani R, Zamboni G, et al. Cystic dystrophy of the duodenal wall: radiologic findings. *Radiology* 1997;**205**:741-747.
11. Rebours V, Lévy P, Vullierme MP, et al. Clinical and morphological features of duodenal cystic dystrophy in heterotopic pancreas. *Am J Gastroenterol* 2007;**102**:871-879.
12. Wagner M, Vullierme MP, Rebours V, Ronot M, Ruszniewski P, Vilgrain V. Cystic form of paraduodenal pancreatitis (cystic dystrophy in heterotopic pancreas (CDHP)): a potential link with minor papilla abnormalities? A study in a large series. *Eur Radiol* 2016;**26**:199-205.
13. Shudo R, Yazaki Y, Sakurai S, et al. Groove pancreatitis: report of a case and review of the clinical and radiologic features of groove pancreatitis reported in Japan. *Intern Med* 2002;**41**:537-542.
14. Ooka K, Singh H, Warndorf MG, et al. Groove pancreatitis has a spectrum of severity and can be managed conservatively. *Pancreatology* 2021;**21**:81-88.
15. Izbicki JR, Knoefel WT, Müller-Höcker J, Mandelkow HK. Pancreatic hamartoma: a benign tumor of the pancreas. *Am J Gastroenterol* 1994;**89**:1261-1262.
16. Pauser U, Kosmahl M, Kruslin B, Klimstra DS, Klöppel G. Pancreatic solid and cystic hamartoma in adults: characterization of a new tumorous lesion. *Am J Surg Pathol* 2005;**29**:797-800.
17. Muraki T, Kim GE, Reid MD, et al. Paraduodenal pancreatitis: imaging and pathologic correlation of 47 cases elucidates distinct subtypes and the factors involved in its etiopathogenesis. *Am J Surg Pathol* 2017;**41**:1347-1363.
18. Değer KC, Köker H, Destek S, et al. The clinical feature and outcome of groove pancreatitis in a cohort: A single center experience with review of the literature. *Ulus Travma Acil Cerrahi Derg* 2022;**28**:1186-1192.
19. Vitali F, Kiesslich R, Heinrich S, et al. Paraduodenal pancreatitis: mini-series with regard to vessel obliteration. *J Pancreas (Online)* 2012;**13**(5 Suppl):647.
20. de Pretis N, Capuano F, Amodio A, et al. Clinical and morphological features of paraduodenal pancreatitis: an Italian experience with 120 patients. *Pancreas* 2017;**46**:489-495.
21. Casetti L, Bassi C, Salvia R, et al. "Paraduodenal" pancreatitis: results of surgery on 58 consecutives patients from a single institution. *World J Surg* 2009;**33**:2664-2669.
22. Balduzzi A, Marchegiani G, Andrianello S, et al. Pancreaticoduodenectomy for paraduodenal pancreatitis is associated with a higher incidence of diabetes but a similar quality of life and pain control when compared to medical treatment. *Pancreatology* 2020;**20**:193-198.
23. Vitali F, Hansen T, Kiesslich R, et al. Frequency and characterization of benign lesions in patients undergoing surgery for the suspicion of solid pancreatic neoplasm. *Pancreas* 2014;**43**:1329-1333.
24. Triantopoulou C, Dervenis C, Giannakou N, Papailiou J, Prassopoulos P. Groove pancreatitis: a diagnostic challenge. *Eur Radiol* 2009;**19**:1736-1743.
25. Arvanitakis M, Rigaux J, Toussaint E, et al. Endotherapy for paraduodenal pancreatitis: a large retrospective case series. *Endoscopy* 2014;**46**:580-587.
26. Klöppel G, Zamboni G. Acute and chronic alcoholic pancreatitis, including paraduodenal pancreatitis. *Arch Pathol Lab Med* 2023;**147**:294-303.
27. Andrieu J, Palazzo L, Chikli F, Doll J, Chome J. [Cystic dystrophy on aberrant pancreas. Contribution of ultrasound-endoscopy]. *Gastroenterol Clin Biol* 1989;**13**:630-633.
28. Campos LP, Mateu CA, García-Argüelles JS, Durá Ayet AB, Pérez IB, Callol PS. Cystic dystrophy of the duodenal wall: a rare but need-to-know disease. *Endosc Ultrasound* 2017;**6**:61-66.
29. Rana SS, Sharma R, Guleria S, Gupta R. Endoscopic ultrasound (EUS) elastography and contrast enhanced EUS in groove pancreatitis. *Indian J Gastroenterol* 2018;**37**:70-71.
30. López-Muñoz P, Lorenzo-Zúñiga V, Alonso-Lázaro N, et al. Endoscopic findings of paraduodenal or groove pancreatitis. *Endoscopy* 2022;**54**:E735-E736.
31. Tarvainen T, Nykänen T, Parviainen H, et al. Diagnosis, natural course and treatment outcomes of groove pancreatitis. *HPB (Oxford)* 2021;**23**:1244-1252.
32. Banks PA, Bollen TL, Dervenis C, et al; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102-111.

33. Lekkerkerker SJ, Nio CY, Issa Y, et al. Clinical outcomes and prevalence of cancer in patients with possible groove pancreatitis. *J Gastroenterol Hepatol* 2016;**31**:1895-1900.
34. Vitali F, Strobel D, Frulloni L, et al. The importance of pancreatic inflammation in endosonographic diagnostics of solid pancreatic masses. *Med Ultrason* 2018;**20**:427-435.
35. Boninsegna E, Negrelli R, Zamboni GA, Tedesco G, Manfredi R, Pozzi Mucelli R. Paraduodenal pancreatitis as a mimicker of pancreatic adenocarcinoma: MRI evaluation. *Eur J Radiol* 2017;**95**:236-241.
36. Jun JH, Lee SK, Kim SY, et al. Comparison between groove carcinoma and groove pancreatitis. *Pancreatology* 2018;**18**:805-811.
37. Schima W, Böhm G, Rösch CS, Klaus A, Függer R, Kopf H. Mass-forming pancreatitis versus pancreatic ductal adenocarcinoma: CT and MR imaging for differentiation. *Cancer Imaging* 2020;**20**:52.
38. Kalb B, Martin DR, Sarmiento JM, et al. Paraduodenal pancreatitis: clinical performance of MR imaging in distinguishing from carcinoma. *Radiology* 2013;**269**:475-481.
39. Shin LK, Jeffrey RB, Pai RK, Raman SP, Fishman EK, Olcott EW. Multidetector CT imaging of the pancreatic groove: differentiating carcinomas from paraduodenal pancreatitis. *Clin Imaging* 2016;**40**:1246-1252.
40. Itoh S, Yamakawa K, Shimamoto K, Endo T, Ishigaki T. CT findings in groove pancreatitis: correlation with histopathological findings. *J Comput Assist Tomogr* 1994;**18**:911-915.
41. Castell-Monsalve FJ, Sousa-Martin JM, Carranza-Carranza A. Groove pancreatitis: MRI and pathologic findings. *Abdom Imaging* 2008;**33**:342-348.
42. Bonatti M, De Pretis N, Zamboni GA, et al. Imaging of paraduodenal pancreatitis: a systematic review. *World J Radiol* 2023;**15**:42-55.
43. Isayama H, Kawabe T, Komatsu Y, et al. Successful treatment for groove pancreatitis by endoscopic drainage via the minor papilla. *Gastrointest Endosc* 2005;**61**:175-178.
44. Chantarojanasiri T, Isayama H, Nakai Y, et al. Groove pancreatitis: endoscopic treatment via the minor papilla and duct of Santorini morphology. *Gut Liver* 2018;**12**:208-213.
45. Issa Y, van Santvoort HC, Fockens P, et al; Collaborators. Diagnosis and treatment in chronic pancreatitis: an international survey and case vignette study. *HPB (Oxford)* 2017;**19**:978-985.
46. Kager LM, Lekkerkerker SJ, Arvanitakis M, et al. Outcomes after conservative, endoscopic, and surgical treatment of groove pancreatitis: a systematic review. *J Clin Gastroenterol* 2017;**51**:749-754.
47. Egorov VI, Vankovich AN, Petrov RV, et al. Pancreas-preserving approach to "paraduodenal pancreatitis" treatment: why, when, and how? Experience of treatment of 62 patients with duodenal dystrophy. *Biomed Res Int* 2014;**2014**:185265.
48. Rana SS, Bhasin DK, Chandail VS, et al. Endoscopic balloon dilatation without fluoroscopy for treating gastric outlet obstruction because of benign etiologies. *Surg Endosc* 2011;**25**:1579-1584.

Supplementary material

Supplementary Table 1 Diagnostic criteria for diagnosis of paraduodenal pancreatitis (for references see manuscript text)

Patients who underwent surgery	
Histology on operative specimen:	Brunner gland hyperplasia Adenomyomatosis (myoid stromal proliferation) Dilated ducts and intramural cyst or pseudocysts in the duodenal wall Granulation tissue with foreign-body giant reaction Neural proliferation
Patient who did not undergo surgery	
Cross-sectional imaging	Radiological or endoscopic signs of duodenal stenosis Thickening of the duodenal wall >9 mm at the minor papilla level Arterial hypoenhancement of the duodenal wall after contrast medium application, patchy enhancement in the portal venous phase Hypointense relative to the pancreatic tissue on T1-weighted images, and iso or slightly hyperintense on T2-weighted images, delayed contrast enhancement on the late-phase images Duodenal wall cysts (microcyst <1 cm, macrocysts >1 cm) or in the groove Leftward or medial displacement of a normal appearing gastroduodenal artery.
EUS criteria	Duodenal wall thickening, particularly the submucosa and *muscularis propria* (fourth hypoechoic layer) Cysts inside the duodenal wall Loss of wall stratification (in the acute recurrent inflammatory phase) (optional) Hard appearance on elastography after contrast enhanced EUS areas around the cyst are not enhancing and surrounding thickened wall show patchy delayed enhancement

Endoscopic ultrasound (EUS) criteria: Duodenal wall cyst within the submucosa and *muscularis* of the diffusely thickened duodenal wall

MRI: Mass lesion occupying the pancreaticoduodenal groove (hypointense relative to the pancreatic tissue on T1-weighted images, and iso or slightly hyperintense on T2-weighted images); thickening of the duodenal wall; and/or cysts in the groove and/or duodenal wall